Position Paper on Artificial Heart Program of NHLI
as redone for
Robert Ringler

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THE PROGRAM ON THE DEVELOPMENT OF AN ARTIFICIAL HEART

AN EVALUATION

by

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ARTIFICIAL HEARTS AND DEVICES FOR CIRCULATORY ASSISTANCE
OF THE PROGRAM ON THE ARTIFICIAL HEART ON NHLI

SECTION I

HISTORICAL BACKGROUND

During the late 1950's, several men in the United States embarked upon efforts to develop artificial hearts. Among these were Dr. Willem Kolff, Dr. H. B. Shumacker, Dr. Adrian Kantrowitz, and Dr. Michael E. DeBakey. The initial effort was to provide specific components of such devices rather than to support the undertaking as a whole.

In 1963, largely at the suggestion of Dr. DeBakey, the Advisory Council of the National Heart Institute expressed an interest in devices to give circulatory assistance and in artificial hearts. The Director of the NIH, Dr. James Shannon, asked Dr. Ralph Knutti, Director of the National Heart Institute, to appoint an advisory group on the mechanical heart. This group met on February 21, 1964, and consisted of the following men: E. C. Andrus, M.D.; M. E. DeBakey, M.D.; Ben Eiseman, M.D.; Willem J. Kolff, M.D.; John R. Beam, M.D., Associate Director for Program Planning and Scientific Information, NHI; Robert L. Bowman, M.D., Laboratory of Technical Development, NHI, Intramural; Eugene Braunwald, M.D., Chief, Cardiology Branch, NHI, Intramural; Joseph W. Gilbert, M.D., Deputy Chief, Surgery Branch, NHI, Intramural; C. William Hall, M.D., NHI; Philip Janus, Program Planning Officer, NHI; Ralph Knutti, M.D., Director, NHI; and James M. Stengle, M.D., Office of Program Planning and Evaluation. NHI, Extramural. After extended study, the group recommended encouragement of work in this area, including the making of contracts with industrial groups and the assignment of staff and consultants as necessary.

Initially, Dr. Beam was in charge of this staff. When he departed in 1965, Dr. Frank Hastings, who had joined the staff the preceding year, was placed in charge of the Artificial Heart Program. Dr. Frank Hastings died in March 1971. Dr. Lowell Harmison was Acting Chief of the Branch. From that time until March 6, 1972, when Dr. Dennis was placed in charge, serving in this capacity from March 6, 1972 until August 10 of 1973.

In 1965, contracts were let to six contractors jointly by the NHI the AEC to explore the feasibility of an artificial heart from an engineering point of view, and in 1966 an additional contractor was chosen, Hittman Associates, to integrate the reports of the initial six contractors.[1] The result was a study which became available late in 1966, indicating that an implantable artificial heart was feasible, and predicting that totally implantable hearts could be ready for trial in animals in 1968 and in man in 1970 provided sufficient funds and effort were to be applied.

This report was made the basis of the Artificial Heart Program, later broadened to become the Medical Devices Applications Branch, and in 1972, upon the acquisition of Bureau status by the National Heart and Lung Institute, re-named the Division of Technological Applications. The Division of Technological Applications was dissolved in August of 1973, primarily as a result of financial difficulties resulting from executive impoundment of funds and as a result of the imposition of a personnel ceiling which precluded acquisition of appropriate staff to run such a program. Since that time, the management of the program has resided in the cardiovascular Devices Branch of the Division of Heart and Vascular Diseases, and in the Division of Blood and Blood Resources.

SECTION II

THE MAGNITUDE OF THE NEED FOR AN ARTIFICIAL HEART

A. The Artificial Heart

The rash of cardiac transplantations of 1968 led to the establishment of a special task force to review the matter of cardiac replacement from all angles. The need for cardiac replacement was analyzed in great detail. The estimate was made from accummulated figures that the availability of hearts for transplantation would not exceed 22,000 in the United States per year. If the assumption is made that emergency circulatory support equipment has been developed and generally available and if one limits the consideration to patients under 65 who come into the hospitals at least an hour before demise and who have no other medical contraindications to cardiac transplantation or replacement, the demand was estimated to be at a maximum 32,000 per year. It was clear, therefore, that the supply of hearts for transplantation is not adequate to the needs of even this restricted fraction of patients dying of heart disease. The reader is referred to the report of 1969 on cardiac replacement for further details of the study.[2] (Attachment #1)

If one re-reviews the data presented in the report of 1969 on cardiac replacement in the light of the present widespread availability of devices for giving circulatory support over hours or even days in preparation for transplantation, the demands for cardiac replacement are larger than estimated in 1969. In the earlier estimation, patients in hospital more than one hour in whom sudden or rapid death was unexpected were excluded from consideration. Similarly, those who died with a history of prior severe heart disease within an hour after admission to hospital were excluded. If one takes into consideration the excellence and general availability of resuscitative devices and of devices for support of the circulation not available in 1969, but available today, of the 25 such patients in the combined Framingham and Tecumseh experience it could be projected that 60% or 15 patients might be salvaged. Furthermore, the widespread availability in emergency rooms of equipment to deal with cardiac emergencies combined with emerging studies such as that at Baylor University in which efforts are being made to expedite arrival of resuscitative equipment at the locus of the victim, might well justify the supposition that instead of the salvage of but one of seventeen patients who die outside the hospital more than an hour after onset in the study of 1969 might today be a salvage of six patients. If these extra five patients are added to the fifteen patients estimated above who might now be salvaged who had died in the hospital, the total number of potential candidates for cardiac replacement in the 103 total coronary heart deaths of the 1969 study would be 50 patients or 27% of the entire population in the combined experience. If this number were multiplied by the nationwide estimate of 150,701 deaths under age 65 from coronary disease in the United States in 1967, the high estimate of candidates for cardiac replacement would be not the earlier figure of 26,027 but the figure of 43,337 annually.

B. <u>Mechanical Circulatory Assistance</u>

An entirely different chapter is the matter of the need for devices to give circulatory assistance. The pioneer work of Summers[3] in demonstrating the feasibility of performance of coronary arteriograms on patients in cardiogenic shock with support by the intraortic balloon technique opened up an immense field for such invesigation and was followed by the work of Buckley, Austen, and associates at the Massachusetts General Hospital.[4] The need for more effective means of circulatory support than the intraortic balloon has led several groups to embark upon venoarterial pumping with oxygenation with refined types of equipment. The likelihood exists that such techniques may be used on a very substantial fraction of the more than half-million American citizens who die of arteriosclerotic heart disease, including coronary arterial disease, each year. While it is possible that utilization of such devices and demonstration by coronary arteriography of the feasibility of aorto-coronary bypass might very well reduce the candidates for cardiac replacement, nonetheless the fact that about two-thirds of these patients will be found to have coronary arteriograms inconsistent with aorto-coronary bypass, and these patients then will be in the position of being under mechanical support with no choice in the long run except either to maintain this mechanical support indefinitely or to embark upon cardiac replacement. The likelihood therefore is that the numbers of candidates both for replacement and for prolonged support will be immensely increased.

Applications such as support over several days for patients whose hearts fail to recover expeditiously after otherwise successful open-heart operations are likely to focus the attention of the profession upon the possibilities of prolonged circulatory assistance, but will not in all probability prove to be numerically comparable to applications for coronary arterial disease.

SECTION III

THE SCIENTIFIC PROBLEMS FACED IN 1966

As summarized in the Report on Cardiac Replacement of 1969[2], the major problems faced by the developmental program were essentially as follows.

A. Materials to contact blood and other tissues

This was recognized as the largest of the obstacles and the one requiring the greatest amount of basic research, for the technical knowledge and scientific data were simply not in hand. It was recognized in the 1969 report that the surfaces in contact with the blood stream must have no deleterious effects on the formed elements of blood or on substances in solution in the plasma. The problems were recognized as complex and rendered even more complex by uncertainties as to the purity of the available materials, not uncommonly hidden behind a shield of commercial proprietary interest. A great deal of the work was concerned with the clotting mechanism per se which was and even now is not well enough understood to be dealt with in this connection. A problem which is a serious one and which was not addressed in the 1969 report is that of the effect of the tissues upon the synthetic materials employed.

B. Power Sources

The second major problem in the view of the reviewers of 1969 was that of appropriate power sources. It was recognized that a totally implantable power source would be a very satisfactory solution if it could be accomplished. Toward this end the utilization of plutonium 238 as a source of energy for a thermal engine and the use of biological fuel cells were thought to offer great promise. Thermal engines continue to offer promise, while the feasibility of sufficient power from fuel cells has not been demonstrated.

The provision of power from outside the body was recognized from the beginning as highly disadvantageous because it necessarily requires anchorage of the subject to an external device and because of the difficulties of transmission of power into the body. The utilization of percutaneous cables for either hydraulic, pneumatic, or electrical power was known to be fraught with a prohibitive rate of invasion of infection along those conduits.

C. Pumps

Blood pumps were then considered to be third in the order of importance among the scientific problems, but the magnitude of the problem had not been initially appreciated.

D. Biological Problems

The physiological, hematologic, and biomaterials problems were recognized but were so underestimated as to have proven a major factor in causing the program to lag behind the expectations of the Hittman Report[1].

SECTION IV

THE CHOSEN PATTERN OF MANAGEMENT

The chosen pattern of management is nicely reviewed in the Hittman Report[1], and the 1969 Task Force Report[2] states "The National Heart Institute, under the Directorship of Dr. Knutti, adopted a systems analysis approach in 1966 in order to direct and coordinate the Artificial Heart Program. This approach was intended to make feasible the mobilization of resources of industry, medicine, basic science, engineering and systems management, as needed, to implement any particular aspect of the developing program. After consultation with members of NASA, Air Force Strategic Command, the Department of Defense, and others within the National Institutes of Health, an Artificial Heart Program, based largely on contractual relationship with outside institutions and agencies, was created to define goals and to coordinate research activities." There continued to be support of efforts through the regular granting mechanisms of the National Heart Institute.

In the Artificial Heart Program proper, a small professional staff with three engineers, one surgeon, and several additional physicians undertook to be responsible not only for planning, organizing, and managing the program, but also for monitoring more than 100 ongoing contracts (by 1960). It was also responsible for issuing requests and reviewing proposals for new contracts and concurrently trying to manage a wide variety of other analytical and administrative responsibilities.

An advisory committee was created, and in addition the program convened *ad hoc* technological advisory groups as needed.

Until April 1969, the Artificial Heart Program focused on the separate development of each of the components of the artificial heart rather than on a composite device. In April, 1969, direction shifted somewhat in that a concerted effort was begun to combine the devices and techniques which had been developed under the Program in order to create a complete fully implantable device for cardiac assistance to be used in animals. The thesis was that through the use of this first-generation model a realistic data base could be obtained for the development of subsequent models; many prevalent theoretical concepts concerning design could be put to practical tests; meaningful limits for time and cost of developing the total prosthetic device could be obtained; and the important problem of relating individual components to each other could be given impetus.

In addition to the contractual support, several program project grants were made by components of the National Heart and Lung Institute apart from the Artificial Heart Program. These are not considered in the present report. The annual funding by the grant mechanism is estimated to be $1,272,462 for both work on the artificial heart and on circulatory assistance.

Footnote:
Parallel with the program in the National Heart and Lung Institute, a program has been in progress under the auspices of the Atomic Energy Commission, directed by Dr. William E. Mott. While the NHLI program has developed two types of nuclear powered Stirling engines and one tidal regenerator engine and is currently working upon a rotary powered generator with thermal power source, the Atomic Energy Commission has concentrated upon a standard pattern of Stirling engine with a Scotch yoke type of crankshaft, a fly wheel, and mechanical delivery of power from the engine to the actuator of the pump. All of these devices have worked satisfactorily during bench tests. Those in the NHLI's program have been implanted into animals, and calves have gone as long as 111 hours with left ventricular support pumps running upon nuclear thermal energy. In the Atomic Energy Commission's program, bench testing is highly satisfactory, and it is anticipated that, if the program were to continue, successful bovine implantation would take place within the next eight months.

Since the spring of 1972, close relations have again been established between NHLI and AEC to assure a free interchange of information and thus to accelerate progress.

SECTION V

THE COSTS WHICH HAVE BEEN INCURRED AND OBLIGATED

Break down of the costs according to catergories is a bit difficult because computer retrieval concerning contracts no longer in force is under a somewhat different classification from that in use at the present time. Table I indicates the numbers of contractors, the categories into which they fall, and the costs for contracts no longer in force or which have been moved to the Division of Blood Diseases and Blood Resources. For these latter, Table I includes costs only up until the transfer to the Division of Blood Diseases and Blood Resources.

The program plan of the Cardiovascular Devices Branch of the Division of heart and Vascular Diseases of June 1, 1974 summarizes the costs of the entire program as far as contracts currently in force are concerned. These data are presented in Table II.*

For these particular contracts the total expenditure to the end of fiscal year 1975 (including the item on Test and Evaluation Facilities committed to 1980) is $57,256,509. This, combined with the sum of the figures in the preceding table amounts to a total expenditure bygone, present and legally committed of $80,309,365. It should be noted that this figure does not include artificial heart work supported by the National Heart Institute before the launching of the Artificial Heart.

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* The use of this updated plan of the Cardiovascular Devices Branch is preferable to use of the updated Five Year Plan in the First Annual Report of the Director of NHLI, for the latter (page 50) is confusing and duplicative. Furthermore the back and projected costs have been calculated on the basis of the updated plan of CDB by that Branch as reorganized and portrayed in Table II.

TABLE I

The Costs of Contracts in the Artificial Heart Program which are no longer in force or which have been moved to the Blood Division and continued* **

Category	Number of Contracts	Cost
Devices for circulatory assistance	39	$11,493,467
Artificial heart	3	855,009
Biomaterials, research and development	52	7,016,331
Biomaterials, evaluation	6	2,087,758
Auxiliary devices	2	518,933
Technical Studies	1	19,852
Bioinstrumentation related to AH	6	1,061,506
	TOTAL	$23,052,856

* Data presented on this and the following table do not include:

1. Work funded by grants
2. Work contracted before FY 1968
3. The six original contracts on feasibility (1966)
4. The Hittman synthesis of those six contracts (1966)
5. Contracts on oxygenators or respiratory diagnostic or measuring devices
6. Contracts on instrumentation unless specifically as components of circulatory assist devices or artificial hearts
7. Contracts on biomaterials not directly related to the artificial heart

** On the contracts transferred to the Blood Division, the costs listed here are only those prior to that transfer. Subsequent costs for those contracts are listed in Table II.

TABLE II

COSTS OF CONTRACTS CURRENTLY IN FORCE FROM THE START THROUGH FY 1975

Category C	Cummulative Costs* To FY 1974	FY 1974 Costs*	Projected FY 1975 Costs	Committed Beyond 1975**	Total Costs	No. of Contracts
Blood pumps	$ 4,325,284	$ 1,377,397	$ 1,870,000	-	$ 7,572,681	8
Power sources, nuclear	8,707,820	2,613,209	2,750,000	-	14,071,029	5 (1 term.
Power sources, electric	2,502,560	732,796	1,300,000	-	4,535,356	4
Transcutaneous delivery of power & power source	1,347,389	157,355	0	-	1,504,744	1 (term.)
Applied biomaterials	1,462,797	402,393	540,000	-	2,405,190	4
Basic biomaterials***	****	2,561,962	2,710,252	-	5,272,214	31
Test & Evaluation Facilities	10,981,897	1,359,783	450,000	3,920,000 @	16,801,680	2 (2 term.
Arteriosclerotic pigs	226,579	48,290	6,000	0	280,869	1 (term.)
Fabrication contracts	2,189,390	663,090	900,000	-	3,752,480	2
Thermal dissipation	758,261	182,005	120,000	-	1,060,266	1 (term.)
TOTAL					$57,256,509	

*Data from Program Summary of Cardiovascular Devices Branch of Division of Heart and Vascular Diseases, June 1, 1974, of contracts active in FY 1974 and review of Annual Reports of old Division of Technological Applications from July 1, 1967 to FY 1974, checking amounts where feasible by computer through the courtesy of the Reports and Evaluation Branch of the Division of Extramural Affairs.

**Includes only those legally committed. The second years of the 2-year contracts approved in FY 1975 are not listed because they can be terminated at the pleasure of the government and the support for the second year has not yet been appropriated.

***Monitored in the Division of Blood Diseases and Blood Resources.

****See preceding table for total data on biomaterials from 1967 until transfer of all but four contracts to the Division of Blood Diseases and Blood Resources late in 1973 (Oct & Nov)

@Committed rental and upkeep for balance of 10-year contract on one facility (to 1980) it include the seventh contractor (Hittman Associates) brought in to synthesize the reports of the first six, nor does it include the cost of the *ad hoc* task force on cardiac replacement in October of 1969, nor does it include the costs of the Artificial Heart Assessment Panel of 1973, nor does it include work supported by grants. Finally, there were some contracts concerning which it appeared impossible to retrieve the data from early in the program.

The figure of $80,309,365 therefore represents a minimal figure.*

It should be stressed that not everything which was included in the initial Artificial Heart Program, in the Medical Devices Applications Branch, and in the Division of Technological Applications has been included in this figure. Specifically, all work on pulmonary monitoring and diagnosis and all work on instrumentation not clearly directly related to the instrumentation needed for success of an artifiicial heart have been eliminated from the calculations of total cost (See Table I).

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*The 1973 Fact Book of NHLI lists costs from inception of $70,227,000. This, however, includes items specifically omitted in the present report.

SECTION VI

THE SCIENTIFIC STATUS TODAY

The present status of the scientific development in the Artificial Heart Program can hardly be extensively reviewed in a report such as this, if for no other reason than that the author has expertise only in certain areas of the overall program. The present status therefore will be for the most part descriptive rather than intricately critical.

A. Implantable pumps for blood

Table III shows the present status of work on pumps for blood both in and out of the contractual program on artificial heart of NHLI. It is noteworthy that only one of this list of groups has thoroughly studied the patterns of blood flow within pumping chambers, and this particular establishment carried out these studies before being contractually tied to the Artificial Heart Program. It is also noteworthy that only two groups have done meticulous studies as to the size, shape, fit, and weight of the artificial heart, and both of these groups were working quite independently of the organized Artificial Heart Program. Of those five which have done a fair amount of work, but somewhat less than contractors No.1 and No. 3 in Table III, contract No. 2 is being guided by Dr. Sylvain Pitzele in the office, contractors No. 5 and No. 13 are also supported by the AEC; contract No. 8 did these studies in advance of support by the Artificial Heart Program, and only contractor No. 7 within the Program carried out these studies under that support. It is ironic that this contractor, No. 7, has lost his support from the Artificial Heart Program.

It is also clear from Table III that thus far it is only those pumps with pneumatic drive which appear to have been reasonably satisfactory from the point of view of physiological performance.

One contractor has replaced the ventricles of a calf with man-made ventricles and achieved survival for 95 days[5]. The lethal factors are not well understood, but advance of infection from outside the body along the percutaneous leads is an important factor. Efforts are being made to

TABLE III

PUMPS UNDER DEVELOPMENT IN AND OUT OF THE CONTRACTUAL PROGRAM
ON ARTIFICIAL HEART OF NHLI

Contractor	Type of pump	Actuator	Rheology well studied	Blood interface	Size and fit well studied	Quality of controls	Physiologic performance
(1)	Sac-type	Mechan	+	Smooth silastic	++++	Not yet	Unproven
2	Axisymmetric	Hydraul	?	Smooth	+++*	Not yet	+
(3)	Sac type	Pneumatic	+	Pseudo-intima	++++	+++	+
(4)	Sac type	Pneumatic	0	Smooth	++	++	+++
5	Sac type	Pneumatic	+	Smooth	+++	+	+++
6	Rotary	Electro-magnetic	++	Smooth	+	Not yet	?
7	Sac type	Pneumatic	?	Smooth	+++	+++	++++
8	Sac type	Pneumatic	++++**	Smooth	+++	+	++++
9	Pusher plate	Hydraulic	0	?	+	++	Unproven
10	Axisymmetric	Pneumatic	+	Pseudo-intima	+	+	+++
11	Pusher plate	Hydraulic	0	Pseudo-intima	0	+?	+
12	Axisymmetric	Pneumatic	0	Pseudo-intima	+	+	+
13	Sac type	Pneumatic	+	Smooth	+++	+++	++++

* Arranged by Dr. Pitzele of the Program Office.
** Penn. State's rheologic studies were performed before the start of support by the Program, supported in part by grants from NHLI.
( ) Indicates work not funded by the contractual program on the Artificial Heart
1.= AEC; 2.= Andros; 3.= Baylor Univ.; 4= U. of Cal, S.F.; 5.= Cleveland Clin.; 6.= Univ. of Minn.; 7.= Univ. of Miss.; 8.= Penn.State; 9.=TECNA-Mini-H-TAH; 10.= TECO-CHMC; 11.= TECO-H-Tah; 12.= TECO-THI; 13.= Univ. of Utah.

TABLE IV

POWER CONVERTERS

Contractor**	Proposed Source of Power	Type of Converter	Efficiency	Status	Cost Thru FY 75
1	Pu^{238}	Stirling	19%	Active	$3,823,000
2	Pu^{238}	Stirling	8.9%	Term '71	249,000
3	Pu^{238}	Stirling	?	Term.'73	1,150,000
4	Elect.	Solenoid	60%	Active	1,687,000
5	Pu^{238}	Stirling	19%	Active	3,993,000
6	Elect.	Piezo-el.	?	Active	869,000
*7	Elect.	Rotary-el.	?	Term.'74	1,505,000
8	Elect.	Rotary-el.	?	Active	1,863,000
9	Pu^{238}	Tidal regenerator	11%	Active	4,272,000
10	Pu^{238}	Rotary Rankine	?	Active	797,000
11	Elect.	Electrolytic generator H2	?	Term.'74	117,000

*This initially concerned only transmission of power through the skin

**1 = Aerojet; 2 = Airproducts & Chem.; 3 = Arco Nuclear; 4 = Andros; 5 - McDonnell-Douglas; 6 = Physics Int'l; 7 = Stanford Res. Inst.; 8 = Statham; 9 = TECO; 10 = TRW; 11 = Tyco Labs.

dissect the problem

B. Power Sources

1. Power Converters

The Artificial Heart Program has supported six contracts with an eye to utilizing the thermal energy of degeneration of plutonium 238. It has in addition supported five electrically driven converters. The types of converters, the efficiency of the various devices, and the costs are indicated in Table IV. Further discussion on the relative merits of the thermal engines appears in Section VII, Subsection A.

2. Delivery of Electrical Power to the Implanted Device

As far as the electrical drives are concerned, there is currently a rather unsettled state of affairs in that the patterns by which electrical power can be delivered into the body appear not to have been satisfactorily resolved. For a time the electro-magnetic transfer of power through the intact skin in the hands of contractor No. 7 above appeared to be very satisfactory. Long-term trials of this technique proved however to be fraught with difficulties, and this pattern has been abandoned. An earlier effort by a different contractor was terminated in 1969. Yet another aspirant for support with twelve years experience and rather singular success failed to achieve funding from NHLI (The request was made through the grant mechanism). This matter is further discussed in Section VII, Subsection A.

The other pattern of delivery of power to a subcutaneous position lies in the development of percutaneous conduits of such nature that infection from outside the body cannot extend along those conduits to contaminate the area of the device, a catastrophic complication. An earlier contractor appeared to be gaining success, but the contract unfortunately was terminated. One contractor (TECNA) at the present time appears to have been successful, at least in small animals. Several workers outside the Program appear to have made devices for this purpose which are satisfactory. This matter is discussed also in Section VII, Subsection A.

3. Thermal Dissipation

Another integral component of the problem is that of dissipation of that portion of introduced power as heat which is not successfully converted to the pumping of blood. The magnitude of the need for dissipation is of course greatest in the thermal engines. The problem of this dissipation appeared to have been resolved by one contractor, although it involved the necessity of placing a heat exchanger in continuity in the descending aorta, an added surgical manuever which it appeared advisable to avoid. The problem of dissipation of heat continues. This matter likewise is further discussed in Section VII, Subsection A.

C. Biomaterials

When the Division of Technological Applications was disbanded in the summer of 1973, four contracts concerning biomaterials remained with the rest of the Artificial Heart Program and were transferred to the Cardiovascular Devices Branch of the Division of Heart and Vascular Diseases. The remainder of the contracts were transferred to the Division of Blood Diseases and the Blood Resources. There are now in that Division thirty contracts and three reimbursable agreements. Twenty-eight of those contracts and the three reimbursable agreements are directly concerned with the program on the artificial heart. The four contracts in the Division of Heart and Vascular Diseases are concerned with the pseudointima, three of them with development of the most effective microfiber surfaces for the attachment of intimal cells in culture and the fourth one in the culture process proper.

Table V shows the distribution of effort among those twenty-eight contracts and three reimbursable agreements concerned with the Artificial Heart Program in the Division of Blood Diseases and Blood Resources.

In all of this, the major problem revolves around the interaction between synthetic materials and tissues, including blood. To the present time, the only surface which appears to be tolerated by the blood is the rigid pyrolytic carbon developed at Gulf Atomic. This requires a rigid substrate to

TABLE V

Contracts and/or tasks in contracts on the study of basic biomaterials in the Division of Blood Diseases and Blood Resources

Study of interaction of components of blood with specific components of tissues which might be used as the basis for a synthetic interface

Elastin	2
Collagen	5
Aortic Basement Membrane	2
Endothelial Surface Coat	1
Fibroblasts	1
Smooth Muscle	1

Testing of Materials for Biocompatibility

Ex vivo	1
In vivo	2

Rheology of Thrombus Formation	2
Systemic Hematologic Responses to Materials	1

Thromboresistant Surfaces

Heparin-chondroitin-6-sulfate	1
Hyaluronic acid	1
Bound Heparin	1
Hydrogels	5
Development of ion beam deposited carbon on biomaterials	1
Studies of carbon-surfaced polymeric, metallic, and ceramic biomaterials	1

Erosion of Biomaterials by Shear	3
Influence of Biomaterials on Hemolysis due to Shear	1
Interaction of Blood Proteins with Materials	5
Interaction of Platelets with Biomaterials	1

Synthesis of biomaterials

Anisotropic Materials for Replacement of Valves and Arteries	1
Techniques of Polymerization of surfaces	2
Diverse Polyetherurethanes	2
Springy Polypropylene	1

Pseudointimas and the substrate for same	2*
Evaluation of products of other contractors to predict the behavior of them in advance of implantation	1

*There are also four studies on pseudointima under contract in the Cardiovascular Devices Branch avoid cracking. All flexible surfaces thus far appear to be productive of microemboli or, in the case of microfiber bases for pseudointima, productive of layers of tissue which are not consistently thin enough to permit proper nutrition from the moving blood.

A further aspect of the interrelations between tissues and synthetic materials is the tendency toward fibrous encapsulation of surfaces which provide compliance for adjustment to variations in diastolic filling of synthetic ventricles such that that compliance is presently largely lost.

There are promising developments under investigation. One of these is concerned with initial apparent success in deposition of carbon on flexible synthetic material in such fashion as both to lead to thromboresistance and to facilitate the growth on that surface of pseudointima. Another is concerned with the various hydrogels. These substances have insufficient inherent strength, but there is considerable promise in making coatings of hydrogel upon synthetic substrates and making interlacing networks of hydrogel and other flexible materials.

Perhaps one of the most predictably useful undertakings is that of the Jet Propulsion Lab, which has set up a program of detailed characterization of the products of other contractors with a carefully consideration evaluation of the behavior to be expected in the tissues upon implantation.

D. Test and Evaluation Facilities

The two Test and Evaluation Facilities were established in 1969 and 1970 respectively at a time when it was anticipated many devices would become available for evaluation by impartial scientists. The flow of new devices for evaluation was much less than anticipated, and the cost of operating the T & E Facilities did not therefore seem justifiable. Both have been phased out of the Artificial Heart Program, although one of them is doing some work on contract for the Program.

E. Arteriosclerosis in Mini-pigs

This contract was initiated in fiscal year 1969. The contractor is able to produce arteriosclerosis in mini-pigs, and this was used as a basis for acoustic identification of abnormalities of flow which it was thought might be valuable in monitoring artificial heart devices. This is being phased out.

F. Fabrication

There are two contracts for fabrication of devices already developed and for the use of other contractors. Both of these continue busily.

G. Radiation

For purposes of completeness it is well to present the present status of the understanding of the effects of radiation upon the subject and those about him. The conclusions of a study by the AEC were presented at a joint review of the plutonium-powered artificial heart between AEC and NHLI on April 23, 1973[6][7]. This material is currently being prepared for publication. The data are presented in Table VI.

In the studies on the effects of radiation-equivalent sources upon implantation into experimental animals, one dog has now developed multicentric alveolar carcinoma of the lungs at the end of six years of such radiation. It is difficult to evaluate the import of this observation, for this is a common type of neoplasm in the dog, and the radiation has played a role which is not at all clear[8].

TABLE VI

RADIATION DOSES IN REM/YEAR

Maximum annual safe exposure[7]	0.5
Whole body dose of recipient of nuclear artificial heart	55.0
Dose to spouse of recipient - separate beds	0.7
- same bed	9.0
Dose to other members of the family	0.2
Average dose to each member of the general population estimated for the year 2000 and estimated 188,000 implants	0.0008
Average annual dose to the U. S. population today	0.182
Number of defective children, estimated to be born in the year 2000	2500-5000
Number induced by 188,000 nuclear artificial hearts	25-70
All Cancers in the year 2000 - spontaneous among 188,000 recipients and those about them - recipients	300
- spouses	200
- family of recipient	230
- general population	435,000
Induced cancers - recipients	?
- spouses	15-200
- family of recipients	5
- general population	40

SECTION VII

THE OBSTACLES TO FULL EFFECTIVENESS

Scientific and Managerial Factors

Research and development under systems engineering have blossomed in those areas in which the basic technology was already well in hand. This has been true of the thermal and electrical engines in general and in the development of electronic circuity for control insofar as the basic physiology has been understood. It has too often failed in areas in which the basic scientific knowledge had still to be gained, as in physiological responses, rheology, and materials of appropriate longevity and compatibility with tissues and components of blood.

Obstacles to full effectiveness of the targetted contractual program for development of an artificial heart and devices for circulatory assistance appear on retrospective examination to have been clearly recognizable as early as 1966 when six contractors explored the feasibility of an artificial heart and a seventh endeavored to harmonize the reports of the first six. The conclusions reached then indicated that the totally implantable total artificial heart would be available for implantation in animals in 1968 and that a device appropriate for clinical application would be ready by 1970. This analysis and this prognosis were based on conclusions drawn by groups with incomplete expertise in regard to physiological problems, in regard to hematological problems, in regard to synthetic polymers, and in regard to a host of additional biological problems, the understanding of which at that time was even more incomplete than it is today.

An effort has been made to separate examples of failures in the program into those secondary to scientific misconceptions and those related to managerial judgmental errors. Efforts to make a sharp distinction between these two have not been successful because in each instance one leads to the other and the two become inextricably intertwined. A few examples of some of the difficulties which have arisen will clarify the matter of the extravagant ineffectiveness of utilization of a pattern of systems engineering in development involving basic research.

May 27, 1975. At the request of the Acting Director/NHLI/ NIH this section has been re-done to provide more documentation. Any other pages changed to harmonize are so dated.

A. The Nature of the Problem - Examples

1. Size, Shape, and Weight of the Artificial Heart and Assist Pumps, and the Rheology of Pumps.

One of the cardinal requirements for a device to be implanted within the chest of a living animal or man is that the device must have a shape, size, and weight compatible with such placement. The entire program in the National Heart and Lung Institute insofar as this reviewer has been able to determine has been carried out until recently with no such study on the major animal used in the program, namely the calf, and no such study in man (and this even though a revision of PH43-67-1116, Modification #13, Article I, item 9, March 1, 1971, called for just such a study). (See Attachment 2). A thorough study was done on sheep by W.D. Anderson of the University of Minnesota (Contract No. PH-43-68-1337). The Annual Report of the Artificial Heart Program for 1969 to 1970 states, "The purpose of this program was to study the anatomy and illustrate the gross morphology of the ovine thorax and associated structures, with emphasis on cardiopulmonary vasculature of this species." This contract was terminated on August 31, 1969. From a sound programmatic point of view, why were the studies contracted with Thermo-Electron on Mar. 1, 1971, not carried through to application to the artificial hearts and assist pumps developed in the Program? The H-TAH does not appropriately reflect such studies. Such studies were done under the auspices of the Atomic Energy Commission for the calf, although miniaturization will be needed for clinical application. Also, neither program appears to have given adequate thought to the fit of the engine.

In contrast to the AEC, the Program of NHLI developed, primarily with direction from within the Program Office, the H-TAH. The author has not been able to view the records, if any, of study of the proposed pump by a review group, since his departure from NIH Nov. 30, 1974, renders him no longer eligible to view such records, even though it might prove helpful to the effectiveness of this "Evaluation".

A letter from Dr. Walter Bornhorst of TECO disclaims knowledge of review by a review group (Attachment 3). Now that great sums have been spent on this pump and the result has proven unsatisfactory, it is fruitful to examine insofar as presently possible the mechanisms under which this step was taken in order that this pitfall may be avoided in the future.

There appears to be some uneasiness, for Dr. Bornhorst's letter of April 25, 1975, in response to an inquiry from the writer, states, "The initial concept of the direct activation LVAD which later became known as the H-TAH pump was first proposed to the NIH by Thermo-Electron on Oct. 7, 1970". The letter does not say the concept was generated by TECO, and the fact that it was named the Harmison-Total Artificial Heart (H-TAH) strongly suggests that the concept arose in NHLI, especially since the engineering drawings were drawn by Dr. Harmison.

If such is the case, would it not have been better policy to issue an RFP for development rather than to add it to a contract for fabrication of developed devices for the use of other contractors? (Attachment 2, TECO Contract PH43-67-1116, Modification 13, effective Mar. 1, 1971, Article I, item 6). This would have provided open competition, and hence probably greater expertise would have been applied.

Finally, no meaningful studies were done on the effects of size and shape until insisted upon by Dr. Pitzele in 1973-1974. As indicated in the Annual Report of TECO on Contract No. HT-4-2910, Report No. 4183-14-75, p. IV-14, Table IV-1 (Attachment 4), five dummy pumps of the size and configuration of the H-TAH placed in five calves killed them all, and a compliance bag of Medical Grade Silastic adhesive (A) placed in the abdomen resulted in massive local necrosis sufficient to nullify the information sought on effects of pulsing on neighboring organs. This adhesive had been used almost routinely to encase pumps and engines for implantation without apparent appreciation that polymerization releases enough acetic acid to produce necrosis. Would this point not have been foreseen by a competent review group, a monitor with appropriate expertise, or a top-flight investigator?

2. Thermal Dissipation

Another example has to do with the problem of thermal dissipation. This problem was attacked by Dr. M. Gillis at Battelle Northwest Laboratories under contract PH-43-66-1130. The reports of the Program Office indicate, "That the electrically energized heaters were designed with an extended area to be in contact with descending aortic blood flow. This was fitted with a nonthrombogenic pyrolytic graphite coating and was finned to give a maximal surface to contact the flowing blood. Such a heater attained eighteen months of continuous heating at 69 watts with no clinical or postmortem evidence of deleterious effect. Most significantly there were no signs of downstream thromboembolic phenomena, further testifying to the excellent blood compatible properties of this surface treatment." These devices were implanted, and the animals were maintained throughout subsequent experimental periods, during which heater power and internal transducer feedout were provided by percutaneous leads. "The results of this work are as follows: In the absence of high ambient temperature or systemic infection causing fever, miniature swine will tolerate 60 watts added heat for 24 to 36 months without overt alteration of physiologic functions. Specific heat input rates to the group of heated animals in the chronic study ranged from 0.16 to 0.9 watts per kilogram of body weight. Flux at the heat transfer surface is 4.7 watts per square centimeter." This contract was terminated in June, 1973.

A simultaneous study on dissipation of excess thermal energy was performed under the auspices of Thermo-Electron Corporation (Contract No. PH-43-66-982). In this project, the effort was made to dissipate heat through the pump bladder. There was a great deal of difficulty with such thermal dissipation. For instance, the pump bladders were covered with flocking in the hope that a "pseudointima" might develop on this surface. Under no circumstances have living cells been found on such pump surfaces through which thermal dissipation has been undertaken. Unfortunately, the pyrolytic carbon utilized by Gillis is brittle and the surfaces to which it is fitted must apparently be rigid rather than flexible. It is perplexing that $1,155,402 was expended on this study on thermal dissipation involving the H-TAH pump designed for the purpose without there being evidence in the Program of a single trial utilizing a device dependent upon thermal dissipation through a pyrolytic carbon surface, until Dr. Pitzele's entry on the scene.

After failure of the H-TAH (see above), a feasibility study was done, with Dr. Peter Richardson of Brown University as consultant, to see if the hydraulic axisymmetric Model X could replace the H-TAH as a test vehicle for the nuclear engines. The polyurethane bladder proved to be too great a barrier to thermal dissipation. Therefore, at the initiative of Dr. Pitzele, the decision was made to design a new pusherplate pump with thermal dissipation through a rigid component coated with Pyrolytic carbon in which no attempt is to be made to dissipate heat through synthetic polymeric materials. A subcontract has been let to Dr. Y. Nose to determine the shape for a proper anatomic fit, work which Dr. Nose had already been doing under the auspices of the AEC. Upon pinpointing by Dr. Pitzele and Dr. Dennis of the faultiness of the former patterns without proper expertise in the Program Office, this problem is finally being approached in a thoroughly well-ordered fashion. (Attachment 5, Blue sheet, Oct. 18, 1974, Contract No. N01-HV-6-982, "Continued study of the effects of added intracorporeal heat", and memorandum, Oct. 21, 1974, from Dr. Pitzele to Director/DHVD, Request for noncompetitive contract renewal).

3. Electromagnetic Delivery of Energy through the Intact Skin

Yet another area in which the overall Program has suffered from incoordination is that of electromagnetic energy transfer through the intact chest wall. Work on this was initially started by John C. Schuder under Grant No. 2R01-HL-05854, starting in 1960. Schuder succeeded in accomplishing a coupling at 1000 watts, for periods of an hour in large dogs and sought in 1972 to have his program extended to permit him to transmit power at the level of 2000 watts, which with developing implantable electrically driven artificial heart devices should have provided the day's need for energy in about 30 minutes. The Cardiovascular and Pulmonary Research Study in Section B rejected this request for renewal because of absence at that time of a system which could accept the energy which Dr. Schuder's research would provide.

A second investigator, Mr. Dean Porterfield of Hamilton Standard Division (Contract No. PH-43-67-1406), developed an implanted secondary pancake coil and an external primary capable of transmitting more than 30 watts of controlled power across the intact skin at a frequency of 522 kilohertz (Schuder had used 428 kilohertz). This system performed satisfactorily while in operation, but there was difficulty with breakage of leads and with encapsulation. Although the precise placement of the primary coil is critical, the

Annual Reports of the Artificial Heart Program do not make mention of this having been a difficulty in Porterfield's device. This program was terminated on November 26, 1969, apparently because of the problems with breakage and encapsulation.

A third study on transcutaneous power transmission was that of the Stanford Research Institute (Contract No. PH-43-67-1422). This involves a suitcase handle covered with skin by a plastic surgical procedure as part of a closed coil structure in the secondary component of the device, which provides a magnetic path to provide efficient coupling with the primary. Although this device has worked over a range from 20 to 120 watts, studies at the Illinois Institute of Technology this past year indicate that prolonged utilization of this device is impossible because of erosion, necrosis, and infection. (The IITRI renewal proposal, 74-6794, submitted July 29, 1974, but not renewed). The entire SRI transcutaneous power transmission Program has been abandoned for these reasons ($1,504, 744, which also includes an electric power converter, also now abandoned). This contract was continued over six years and was dropped only when studies proposed by Dr. Pitzele demonstrated weaknesses which should have been apparent from the start.

It is as though there were no clear concept of the various patterns of work in progress simultaneously either on the part of the Program Office or on the part of the Cardiovascular and Pulmonary Research Study Section B. The Program is currently left without any satisfactory transcutaneous pattern of transfer of energy.

4. Encapsulation

In the light of the abandonment of the Hamilton Standard pattern because of difficulty with lead breakage and encapsulation, it is interesting to review the progress of Lee Pharmaceuticals (Contract No. PH-43-68-1409). During the first two years of the contract (initially under Epoxylite Corp., a parent company of Lee Pharmaceuticals), a series of polyurethane and epoxyresin materials was developed for insulation of implantable devices of interest to the Program Office. It was considered that the problem had been solved, and it is stated, "In view of the stated lack of need for the encapsulation services of Lee Pharmaceuticals, this contract was terminated on March 24, 1972". (Annual Report of MDAB, 1972). This was an unfortunate development inasmuch as recent work at the Pennsylvania State University indicates that the major problem in development of rechargeable long-term pacemakers lies in the lack of satisfactory encapsulation. This is also a problem in pump implants (A1 above).

5. Percutaneous Leads

A most unfortunate misjudgment of necessities is that involving Epoxylite Corporation (Contract No. PH-42-67-1108), set up for the purpose of development of satisfactory long-term percutaneous leads.

The contractor developed a cylindrical conduit with a subcutaneous fenestrated skirt which behaved in very satisfactory fashion but still had further work to be done. In the Annual Report of the MDAB the statement is made, "This design of percutaneous leads shows some promise, but since it does not require further development at this time, the research and development contract was terminated on August 24, 1969." The lack of availability of satisfactory percutaneous leads, work on which was thus abandoned in 1969, has been the single chief obstacle to long-term success in driving artificial hearts and devices for circulatory assistance by means of percutaneous conduits, and the expenditures aimed at driving artificial hearts without overcoming this difficulty have amounted to millions of dollars.

The problem of delivery of energy to devices implanted within the body is still without solution, as is apparent from three recent memoranda within CDB (Attachment 6). The only successful percutaneous tube developed by the most successful of our contractors' efforts, that of TECNA-Searle, is a dialysis shunt which in man has been effectively implanted in patients for up to 14 months. The latest annual report of Searle (Contract No. N01-HV-1-2035, Feb., 1974 to Jan., 1975) shows that as far as percutaneous vascular, pneumatic, or electrical leads are concerned, everything remains to be done. In vivo trials with percutaneous blood leads all became infected. (It is true that one group with no funding from the Artificial Heart Program has reported a percutaneous device which has functioned without infection in dogs for over 9 months(9).

6. <u>The Veno-Arterial Bypass System</u>

An example of failure to appreciate scientific problems on a broad base is the development of the VAB (veno-arterial bypass system). Like the H-TAH pump before it, this was developed on the fabrication contract with TECO without this reviewer being able to find evidence of evaluation of the plans by an outside <u>ad hoc</u> scientific review group. The question again arises as to whether the concept developed in house and without competitive review, for Dr. Harmison's name was placed on this device also. This device was developed without recourse to available scientific knowledge such as the contract with General Electric Co. (PH-43-67-1121) concerned with studies of blood flow in and adjacent to blood pumps, which was terminated August 29, 1969, with a statement in the Annual Report of the Artificial Heart Program, "Although a need exists for further developing and understanding the basic rheologic phenomena applicable to artificial systems, restricted funding levels would not permit continuation of this effort." A small study on rheology was thus terminated while the Program proceeded to spend approximately $450,000 on a VAB which the smaller study would have indicated to be unsatisfactory in the first place. The VAB was ultimately abandoned for the very reasons being explored by the GE contractor. (Attachment 2; Attachment 7)

7. Thermal Engines

In contrast to the AEC, which in 1970 embarked upon development of a single thermal engine (which is not necessarily the best even though chosen after exhaustive review), the NHI Program was launched with questionably sufficiently thorough investigation and funded several contractors and designs. The contracts which have been active in this area are shown in Table VII.

The multiple approach with insufficient prior investigation has resulted in funding of patterns of thermal drives which should have been rejected outright on the basis of the physiological implications. For instance, Contract No. 3 of Table VII proposed a device to sit on the diaphragm which would cover most of the diaphragm. There apparently was no realization on the part of the contractor or of the staff of the Artificial Heart Program that postoperative failure of the diaphragm to move normally is one of the most important and serious complications during the postoperative period. This contract was terminated in 1973 with orderly phaseout in 1974, a disconcerting decision which was eased by the shortage of funds at that time.

Similarly, contractor No. 2 above, although highly effective, was phased out in 1971. The Annual Report of MDAB states, "This system uniquely incorporates a varied, light displacer unit which imposes minimum inertial forces on the system and permits the use of a self actuator and control mechanism to adjust the speed automatically upon demand. With this direct mode of control, the engine power is varied to meet physiological demands. This minimizes the internal unswept volume, thereby reducing the thermodynamic inefficiencies. The system provides a very compact overall design which yields a high power density energy system. A breadboard engine has been developed and tested. This engine ran in a self-sustaining mode at speeds varying from 100 to 1975 rpm. At 350 rpm, the total heat input was 35.6 watts. These tests showed that a thermal reservoir can be used effectively to store energy from a 50 watt source. The practicality of the actuator concept was also verified. Unlike the constant speed resonance type Stirling engines, this positive displacement actuator has a no-stall characteristic. The combination of the positive drive actuator and very light moving parts results in an engine system capable of very fast response. The system operated at normal design pressures of 1000/1200 psi, showing that high pressure engines with inherently smaller components can be fabricated.....The accomplishments of the present program have added a practical new engine concept. The knowledge gained in low inertia, positive displacement systems operating at higher pressures permits the concept to be considered in mating the Stirling engine with the blood pump. Due to funding limitations this program is being phased out in an orderly manner." Why this one? The progress seemed impressive for a study of feasibility.

As to the remaining engines, review in the spring of 1973 found it possible to eliminate No. 3 above but could not make a decision between the two Stirling engines, No. 1 and No. 4 above, and the review group discussed and suggested a plan by which one more year of funding be provided to permit provision of data sufficient to make a choice between them. The sheets prepared by DEA after this review unfortunately do not make this clear. It is true that the differences in data from bench testing were not clear and that more information was needed concerning potential increases in efficiency and decreases in size if either was ever to be considered for implantation in man.

In the review of June 10 and 11, 1974, with changed direction of the Program, this earlier recommendation was naturally overlooked, and both these contracts were renewed, not for one year, but for two years, on the thesis that the level of funding would not permit a more accelerated pace. No. 5 and No. 6 were similarly awarded contracts for two years. (No. 6 had been critically reviewed by AEC and adjudged not worthy of support.) The cost of the <u>first</u> year of these four contracts alone is $2,750,000.

In contrast, Dr. Wm. E. Mott, who attended the review and was not given the courtesy of input, privately informed the author that for a decision on contractors at the start of the AEC program in 1970, and for a less important decision, the AEC had a group of five consultants before taking TRW and Westinghouse and settling on the latter, and that they worked full-time for three weeks. Several days were required for orientation of this group, and the full group spent at least a day visiting each contestant. He also volunteered that the AEC has expertise which is not to be found at NHLI and suggested a joint staff review of all power sources with consultants who clearly would fill the gaps in the orientation in NHLI. This was done as far as the AEC engine program was concerned at Tarrytown, N.Y., August 21, 1974, with but one staff member of CDB in attendance. No joint review has occurred in NHLI since the suggestion.

There has been in the Program too much of token reviews, such as three to four hours to judge all the thermal engines without group site visits, albeit after delivery of the proposals for renewal to members of the task force, which, it became clear at some meetings, were commonly indifferently studied in advance, and sometimes not at all. Finally, it on occasion appeared that the feeling of some of the <u>ad hoc</u> review group was that the in-house staff had already made the decisions anyway. The result appears to have been the funding of multiple contractors, ostensibly to leave no possible pattern unexplored. The AEC has concentrated on one Stirling engine, the larger version of which has been in service for 20 years. Although there are obvious faults in the AEC system, it is the AEC opinion after sitting in on the two-day review of NHLI engines last June, that the AEC engine is more refined, more efficient, and more likely to endure than any in the NHLI Program.

A thorough data retrieval system and a much more thorough review, including all-day site visits, by a well selected task force might produce far more cost-effectiveness.

8. Clinical Use of Left Ventricular Assist Devices

The drive of two contractors to make clinical evaluation of left ventricular assist devices (LVAD) provides an example of the inadvisability of the effort to direct a contractual program without having it effectively monitored by someone with both expertise and responsibility and authority to exercise it. The monitor in these two cases was Dr. Pitzele, a highly gifted and competent surgical cardiovascular physiologist, but he had not been permitted to apply his expertise to the problems. An elegant special task force met with the Director of NHLI on Oct. 28, 1973, to study and make recommendations upon the devices and proposals for use of them. A highly knowledgeable subcommittee met in December, and there resulted recommendations as to the numbers of experiments and the minimal duration of support by such devices which should precede clinical evaluation. As Attachments 8 and 9 indicate, the required proven duration of reliable function was shortened without consultation with the monitor or with the Special Assistant for Technology/OD, who had been asked by the Director to exhibit a high degree of visibility in the matter, to a period which is not justifiable in the eyes of the author of this position paper. This was done by phone call to the 3 members of the subcommittee. (There is room for difference of opinion, but some expert opinions within NHLI were ignored, the writer's and Dr. Pitzele's. It is not known whether the remaining members of the task force were consulted.)

9. Studies of Effects of Radiation on Animals

The studies on implants of radiation-equivalent sources (RES) were undertaken in what has now been adjudged to have been inadequate planning. A group of six baboons in the program has been the cause of review and the decision that the information to be gained after years of care of these animals is not worth continuance, and the CDB office and a group of consultants are working on a protocol to get what can be learned from them. The opinion appears to be that a far more imaginative set of experiments should have been started, including larger groups of smaller animals half of which should carry the RES, with continuance of well characterized observations on both groups. If this is to be done, it will require years from the present time. (Attachment 5, page 4)

B. Mechanisms of errors of which the preceding are examples

The major shortcoming in the system as it has been operating lies in two factors. The first of these is the attempt to use a pattern of systems engineering in a situation in which the basic scientific understanding and technology are not yet in hand. (This will be discussed in Section VIII.)

The second mechanisms lies in the totally inadequate personnel within the National Heart and Lung Institute to guide such a program. The staff simply lacks both the necessary numbers and the necessary expertise to grasp the many points of scientific precision which must be well in hand.*

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* An example of the ineffectiveness which results from the combination of these two factors is that having to do with external compression counterpulsation. The Division of Heart and Vascular Diseases planned a trial of this device and had a task group in to discuss it during the summer of 1972. It was planned to utilize it in several of the Myocardial Infarction Research Units. Although I hold the patent on the device (through the NIH), I was not asked to participate in the discussions. I learned of the meeting indirectly and asked to attend long enough to point out that the device which the MIRU study was planning to use is not satisfactory and that it would be good judgment to await a much more adequate device which with the help of this program would be ready within months. My advice was disregarded, and the study went ahead in the MIRU's at a cost not known to me. The conclusion was that the method is not definitely helpful. Proper evaluation of the method should have utilized apparatus of acceptable quality. (Patent 3,303,841 - Process and Apparatus for Pressurizing Lower Extremities of a Patient During Ventricular Diastole, February 14, 1967).

This example is cited even though it was not in the Artificial Heart Program because it exemplifies the inadequacy of our decision-making processes, in this instance rather apparently both because of lack of proper expertise in the program in question and because of the failure to use proper expertise which was available in NHLI.

C. Need for expertise among monitors of contracts

Successful scientific investigative work is likely to be accomplished only under the close direction of imaginative, knowledgeable, experienced and able investigators provided with facilities, supplies, and personnel to permit them to be first-personally involved in the work in progress. The program on the artificial heart requires for satisfactory progress monitors with expertise in the following areas;

- Cardiovascular physiology
- Cardiovascular surgery
- Cardiology
- Hematology
- Pathology
- Radiological physiology
- Nuclear engineering
- Electronic engineering
- Hydraulic bioengineering
- Biochemistry
- Polymerchemistry
- Mechanical engineering

Governmental personnel ceilings prohibit the gathering together of a corps with these areas of expertise quite apart from the ceilings on government salary which exist today.

The actual situation personnel-wise in the Artificial Heart Program, including biomaterials as well as the related instrumentation, is one in which there is one polymer chemist, one coagulationist, one cardiovascular physiologist who happens also to be a cardiovascular surgeon. Although the remainder of the staff is dedicated and assiduous, the staff fails to provide the depth of expertise required.

It is true that expert task forces have been gathered to review initial proposals and proposals for renewal or evaluation, but these groups can meet only periodically and cannot give the continuing guidance which is essential if basic scientific investigation is to be successfully executed.

D. Need for opportunities in the laboratory for monitors of contracts

Recruitment of an adequate staff within the National Heart and Lung Institute for the purposes of development of devices for circulatory assistance and artificial hearts is blocked not only by the ceilings on personnel and the ceilings on salary, but also by the lack of opportunity for first-personal involvement in the work in question. Efforts to ameliorate this situation by the acquisition of laboratory space and opportunities close to NIH were frustratingly fruitless even before the Presidential impoundment of funds rendered consideration of this move impossible.

The need for first-personal investigative activity in the laboratory on the part of those who monitor developmental contracts related to the artificial heart was expressed by Dr. Frank Hastings. It was re-expressed by the ad hoc task force which generated the 1969 Report on Cardiac Replacement as follows; "Since the Program has no intramural laboratory facilities for research and development, scientists responsible for its direction are handicapped by the absence of opportunities for first-hand experimental experience." (page 28)[(2)] In the preparation of the present report, several consultants have vigorously indicated the need for laboratory facilities in the immediate vicinity of the monitors so that they could be directly involved. Two of these were Dr. Vallee Willman and Dr. John Waldhausen.

A step in the development of the thesis for first-personal scientific involvement if strong scientists are to be recruited and held is presented in Attachment 4. Although the structure of NHLI has changed since the time of that memorandum, the thesis remains the same. Further input in this direction has not resulted in strengthening the situation because of the ceiling in personnel (See Attachment 5).

E. Restrictions on Travel

In recent months, both the crisis in energy faced by this country and the efforts to economize in governmental operations have led to curtailment in allocations for travel. Thus in a program with a large measure of activity related more to basic scientific investigation than to technological development in areas in which the basic technological information is well in hand, precisely that close participation and supervision essential to success is hampered not only by inadequate numbers of personnel and inadequate expertise on the part of this inadequate number, but also by a supposedly coordinated program which is widely distributed all over the United States in the presence of restrictions in travel which render the needed monitoring and supervision impossible.

SECTION VIII

THE CHOICES

A. Research and Development

While it is possible for a contractor to follow new avenues of research as they become apparent, in the present pattern of organization of the Artificial Heart Program this can properly be done only after conferring with the project monitor. This incurs delays which may defer pursuit of the idea or ideas until they are impaired by loss of enthusiasm or experimental materials or preparations. Further delays often arise from lack of availability, expertise, judgment, or even orientation of the project monitors. NIH is hard put to justify this pattern of procedure, for the salary levels, investigative incentives, opportunities for recognition for input of scientific ideas, and separation from personal involvement in investigative work all tend to fail to attract or hold peronnel with both sound scientific ebullience and productive expertise. This defect has even been compounded by placing men with very little investigative expertise in the position of making scientific judgments involving the work to be done by renowned pioneers. The results have too often been disastrous (H-TAH, VAB, TECNA MINI H-TAH, use of the medical innovations external compression counterpulsation in the MIRU program, the Dow Capillary Membrane Oxygenator, problems in thermal dissipation, and the ill-conceived studies in NHLI on tolerance to implanted radioactive sources.)

It is not possible effectively to direct technical developmental work by the contracting mechanisms without available scientifically able and experienced personnel to monitor the work in progress on a day-to-day basis, and with present personnel policies it clearly will not be possible to recruit or to hold such personnel. The problem is compounded in that in the presence of the occasional personnel with the requisite experience who have been recruited, there is a frightening tendency (whether on the basis of fear or a sense of insecurity or ambition) on the part of career men above them to block them from positions for which they are prepared and in which the program desperately needs them.

In view of the points developed thus far and for purposes of consideration of alterations in patterns of operation which might be maximally fruitful, it is appropriate to list the obstacles:

1. Insufficient numbers of staff for proper program monitoring,

2. Insufficient expertise among that insufficiently numerical staff,

3. Inadequate salary to attract the excellence needed for particularly the basic scientific research required,

4. Absence of the opportunity for first-personal involvement as a means both to attract the required intellects and to keep them whetted,

5. Use of even the scientifically qualified personnel on the staff of NHLI in this area in purely mechanical administrative capacities for which they are not prepared while failing to utilize their area of special expertise,

6. A Civil Service System which prevents the removal and replacement of ineffective and/or uncoöperative personnel (A haven for the unproductive cannot be the nucleus for brilliant advances),

7. Wide geographical distribution of contractors, requiring extensive travel on the part of monitors,

8. Restriction on travel,

9. Absence of a retrieval system for data (both favorable and unfavorable) developed in the program and in the field outside the program,

10. Failure of adequate interdisciplinary collaboration. (Although subcontracting has been done from academic institutions to industrial ones, and although subcontracting has been done from industrial contractors to academic groups, the closeness of the collaboration between these groups has been less than ideal, especially in some areas.),

11. The insatiable urge to go to implantation of devices into animals, primarily calves. (This perhaps should be included under one of the above headings, but it has been such a constant characteristic of the program that emphasis is in order. A small change in one portion of the pump in one laboratory was followed by implantation at a cost to the Program of some $6,000 without initial evaluation on the bench. The Program Office in another instance urgently ordered a series of 56 implants of thermally powered devices without completion of preliminary testing on the bench. (Contract PH43-67-1425, which terminated July, 1973, because of the contractor's refusal to submit a proposal in protest against use of animals in this manner)), and

12. The fallacy of utilization of people in a bureaucratic environment as scientific monitors. (As pointed out by Frederic V. Malek,[10] sound scientific investigation requires effective follow-through, and in government "there is always a crisis to deal with"....that requires "federal managers to turn their attention away from important long-term goals to deal with short-term contingencies").

13. Failure to utilize the expertise of scientists who have been recruited because of that expertise. (In the case of the author, recruitment was on the basis of his background in pumping blood, in surgery, in physiology, and in circulatory assistance. After months of frustration with failure of control of the program, when this situation had just been corrected by transfer out of consistently devious and destructive personnel, the Division of Technological Applications was abruptly disbanded. The author since that disbandment, (August, 1973)

has endeavored to "coordinate" technological development in NHLI with limited success and has been in essence kept busy with a panorama of activities for which he is not particularly well grounded while his areas of expertise and the basis for recruitment of him have been ignored. A similar pattern was applied in the case of a surgeon-cardiovascular physiologist recruited by DTA in January, 1973, whoe expertise was ignored or overridden for nearly a year after disbandment of DTA while decisions were being made against his advice which were foolish and costly (e.g. Mini H-TAH pump)).

The possible steps which might overcome these shortcomings were rather carefully studied. In a discussion with Mr. Lyman Moore initially, he indicated that the program management pattern grew out of military procurement and might have some validity as far as our situation in the National Heart and Lung Institute is concerned. In this the project manager is put in charge of a major program in which several different line elements operate in a parallel fashion. He has authority to demand resources from other lines to be put into lines in which this would appear to be useful. He noted that sometimes this is difficult because of shortages one place or another. This makes the project manager a sort of a prestidigitator-master.

The difficulty which led to this pattern was that there existed in the military a general staff without necessarily the expertise and perhaps also without well pinpointed responsibility. The concept was to fix the responsibility in a precise fashion together with authority to command and direct resources. As far as technological development in the National Heart and Lung Institute is concerned, Mr. Moore suggested the solution might be to set up a project manager to run the whole program regardless of the division. He could be in Heart or he could be in the Director's office. He suggested the possibility that a special corporation might be created. It would be of the "think tank" type with a board of directors and a scientific staff, the latter largely to be full-time, and the selection of them supposedly to come from the Director's office, presumably largely from the coordinator of technological development. It was his thought that the general principles would be set by the board of directors, but that the coordination and supervision of the work of contractors would be the business of the scientific staff, the corporation being under contract with the National Heart and Lung Institute. The scientific staff would be persons of acknowledged expertise in the required fields and in investigation. It was his thought that such a pattern might provide us with the calibers of scientific preparation of protocols guidance, and monitoring needed to do our job of development in a proper fashion.

Orientation concerning the possibilities of systems engineering was sought through several publications which were recommended (11,12,13). With a reasonable grasp of the general thesis gained in this fashion, efforts were made to consult with individuals highly experienced in this field. One observation which came from these studies is that this systems pattern of management is likely to be very expensive, particularly when it comes to the setting up of such a program in the Government, in which the likelihood is that judgments will be made not so much on the basis of the end results as on the basis of apparent activity. Nowhere in the course of reading were any statements found with regard to the possible role of this pattern of management in basic scientific investigation.

Dr. Stuart Bondurant was consulted because of his background of experience with the Air Force and because he used to be a consultant to Aerospace. The Air Force first used Rand Corporation.

Another development under this pattern was that of the ballistic missile, for which General Shriver contracted the management of the operation to Aerospace Corporation.

It did not seem appropriate either to Dr. Bondurant or the author to approach the officers of either Rand or Aerospace initially and perhaps not at all as it is rather likely that one or the other might have felt that the opportunity should be vigorously exploited to seek for his institution the contract in question with the National Heart and Lung Institute. It was therefore the decision that it would be wiser to contact people associated with the Department of Defense and seek to get answers from this vantage point, deferring possible communication with the Rand Corp., the Aerospace Corp. and Mitre.

The first contact in DOD was Colonel Russel E. Hensley. He holds a Ph.D. degree in astronautical engineering from Stanford University and is engaged in getting a Ph.D. in Business Administration in Health Care from George Washington University at the present time. We had many long sessions together and he, Dr. Ringler and I also had a session together. This served his purposes as well as those of NHLI because of his interest in using the artificial heart program for a doctoral thesis toward his Ph.D. degree. Col. Hensley interviewed many people in the National Heart and Lung Institute and some in Building 1 as well. His primary thrust after reviewing the situation was that the use of the systems approach (systems engineering) requires a heavy interdisciplinary measure of collaboration and it requires that the technology to be used must be in hand, i.e., the fundamental scientific problems must have been solved, for the use of a systems approach is efficacious only in developing larger components or structures out of basic building blocks of hard scientific information. In addition, he felt it important that the leadership in such a program must know the impact of its decisions upon all aspects of the program. He noted that in DOD there was a distinct advantage in that there is a rather generous exchange of leaders between industry and the military back and forth, so that each knows the problems of the other and collaboration is thereby improved. Most important he felt was the fact that the program must have feedback so that the program is fully aware of the efficacy or the lack of efficacy of the product in the hands of the user.

Col. Hensley was particularly impressed that in biomedical development there was very little evidence of true interdisciplinary collaboration. An example of insularity of much of the medical profession was the failure of the Lockheed Corporation to be able to centralize the services and the records at the Mayo Clinic because of inability to overcome the isolationism of each component of the medical profession there. He regarded the physician as an unreliable consumer in an unstructured market and felt that we could not have sound organization of such a program without a solid OMB type of expertise in the central cadre.

An hour was spent with Lt. Col. Richard Coffee, a program monitor of the Air Force for Rand Corporation and for Analytic Services Corp. Rand Corp. at the moment has been chartered, (1) to develop the analytic methodology which the Air Force can use to solve concrete problems, and (2) to try to ascertain answers not only for problems which now face the Air Force, but to try to ascertain for years ahead what the problems are which the Air Force will have to face. Rand is therefore a Federal Contract Research Center (FCRC). Rand, Aerospace Corporation, and Mitre provide the expertise which permits the Air

Force to be collectively sufficiently knowledgable to provide monitoring for contractors. The feeling was that the Air Force does not have within it the expertise which can be used to deal with the expertise of those in industry. This arrangement has in general been successful. These concerns thus serve as an interface between the Air Force and industry. This ultimately serves to provide an inhouse expertise in highly disciplined areas, to provide advice in continuing fashion, and to determine if the contractors are providing what the Air Force needs.

Col. Coffee felt that the Artificial Heart Program could be handled by the systems approach more readily than anything else in the National Institutes of Health. He was still a little uncertain as to whether a Federal Contract Research Center is really what NIH ought to be seeking for the artificial heart.

As recommended by Dr. Bondurant, after considerable inquiries consultation was held with Dr. John B. Walsh, Deputy Director of Defense, Research and Engineering (Strategic and Space Systems). Dr. Walsh is a Ph.D. electrical engineer who is in charge of all U.S. military satellites. He is a civilian and the details of his message concerning systems engineering may be found in Attachment 6.

Dr. Walsh emphasized vigorously that systems engineering works satisfactorily only if the basic technology is already known. He noted that in some of the projects with which he has been concerned, basic investigation has been necessary. It was his reaction that if new knowledge were to be uncovered in this fashion it was ordinarily a case of "lucking-out." He estimated that the likelihood of having more than 10% of basic investigational work prove fruitful was very remote under this sytem of management. He noted that the costs of guiding a large project on the basis of systems engineering and the magnitude of the team which must be assembled to do so are too large for universities to handle. Systems engineering is therefore to be found almost exclusively in large corporations in industry. In these programs it is not possible for any one individual to grasp all of the detail, but the top level must have enough of a grasp to be able to coordinate the components.

In regard to the development of the artificial heart, it was Dr. Walsh's opinion that an effort to use a systems engineering approach could hardly fail to result in disaster simply because so much basic investigation must be done which is not susceptible to successful attack by this pattern of management. The advantages of this pattern of management are that these concerns can pay sufficient salaries to recruit top-notch people who will do the work properly. FCRCs are on a guaranteed level of effort, and sometimes there is criticism because it looks to some like simply a way of getting around the Civil Service stipulations as to salary. He felt that the reason for these criticisms revolves around the fact that top level people who have high salaries also are likely in governmentl ȸ have a great deal of power, a combination which is dangerous. In the case of the FCRCs these people do not have much power since the contracts can be terminated at any time at the convenience of the Government.

It was Dr. Walsh's opinion that in the artificial heart program there is so much basic scientific discovery still needed that it is probably an area for the independent investigator rather than for a systems engineering approach. In an effort to solve this problem Dr. Walsh suggested that it might be fruitful for NHLI to get a group of top level systems engineers to review the patterns of management of the program to develop an artificial heart. He suggested specific names of people who might serve on this group. These may be found in Attachment 6.

In response to my question as to whether it is feasible to bring truly top quality expertise in depth from outside NHLI into the day-to-day operation of the program, Dr. Walsh had felt that this was possible but that for the reasons indicated in his discussion it was probably irrelevant. With regard to the question "Can a prime contractor take over the whole program making all subcontractors responsible to him?" Dr. Walsh's answer was "No" with the addition that it would be perfectly all right and easily feasible if all of the basic technology were already in hand. Since that technology is not already in hand he felt that this was not a fruitful course to take.

A half hour was spent with Vice Admiral Eli T. Reich. He has had a great deal to do with systems engineering from the point of view of the military rather than from the point of view of the industrial people working for the Pentagon, such as Dr. Walsh. Admiral Reich appeared to concur in the messages which I had obtained from Dr. Walsh without deviation. Admiral Reich also reinforced the previously obtained opinion that systems engineering is not a fruitful pattern of management of basic investigation.

B. Basic Scientific Investigation

As indicated in the preceding section, experience has been widespread that the likelihood of real progress in basic scientific investigation is immensely greater by the unfettered grant mechanism than by the approach of systems engineering. In this connection, a portion of a letter from Dr. Francis D. Moore, which was incorporated in a report to the Acting Director, NHLI, June 29, 1974, on "The Academic Surgical Community's Estimate of Policy Needs for the National Heart and Lung Institute" is as follows:

> "Before you receive this we will all be meeting together in Hamilton, Ontario.
>
> "However, I can tell you for both of our thoughts, the main thrust of my advice to the NHLI.
>
> "And that is, to keep 'contract research' down to a very minimum. It is absolutely impossible to foster the growth of important new knowledge through the letting of research contracts.

"I was quite shocked recently to attend a meeting of a large number of people interested in one of the National Institutes of Health, only to find that the first few minutes of the meeting were taken up by an impassioned defense of the contract research mode of actually comparing it to the space program.

"It was unbelievable that anyone could be so illiterate as not to have read the innumerable statements by scientists demonstrating the vast difference between an engineering achievement such as the space program, and the discovery of fundamental new knowledge.

"Our contract experience with NHLI has demonstrated the usual pernicious tendencies to maximum interference with the independence of investigators, and the actual stifling of research in new directions."

This same matter has been discussed with Dr. Michael E. DeBakey, and the response was of the same import as the letter of Dr. Moore.

In view of the apparently unanimous opinion among those consulted that the method of systems engineering is an extravagant and unproductive pattern in which to pursue basic scientific research, and in view of the experience within the Artificial Heart Program outlined in Section A above, it would appear that some grant mechanism might well be explored for approaching those portions of the Artificial Heart Program in which there is necessity for uncovering of basic scientific knowledge rather than development of technologies which utilize basic technological knowledge and scientific knowledge already in hand. Among the items which might be so characterized are the following:

1. Materials
   a. Basic studies
      (1) Compatibility with tissues and blood
      (2) Resistance to changes produced by body fluids and enzymes
      (3) Longevity in the tissues (flex life for example)

b. Physiological studies

(1) The role of the pulse and the shape of the pulse

(2) The response of pulmonary function to various types of pumping by artificial hearts

(3) Investigation of the control mechanisms of the normal heart

3. Thermal dissipation

4. Rheology

5. Refinement of synthetic cardiac valves

6. Factors in the aggregation of platelets and in hematologic changes

7. Delivery of energy in the body

a. Electromagnetic transmission

b. Formulation of conduits through the skin which preclude admission of infection to the device

The pattern of coordinated activity which might most reasonably be expected to accelerate development in the field of the artificial heart and provision of circulatory assistance would appear to be the establishment of a sound business relationship between NHLI and a group of scientists of such number and expertise as to cover the full field required for the Program. That group would of necessity have to contain at least one each of the following types of experienced investigators:

Cardiovascular physiologist
Cardiovascular surgeon
Cardiologist
Hematologist
Pathologist
Radiation physiologist
Nuclear engineer
Biopolymer chemist
Biochemist

Hydraulic bioengineer

Electronic engineer and probably

Mechanical engineer

In today's market the acquisition of people of the proper scientific expertise to operate such an interdisciplinary effort would require a salary of the order of $60,000 a year. The salary for these people alone for this agency would therefore be of the order of $720,000 per year. If one calculated 50% supplementation for accessory assistance this would be $360,000 and if one provided one-half million for laboratory supplies and facilities the total would be approximately 1-1/2 million for the running of this particular component of the program, once it was equiped and operative.

The agency in question should ideally be empowered and be funded to subcontract those components of the overall program judged by this group of experts to have the basic scientific technology well in hand and to be in need of the commercial type of research and development not available in nonprofit-making institutions. It is also possible that the basic scientific investigative work in such areas as biomaterials might be handled through this primary agency. If there were not to be subgrants as well as subcontracts through this primary agency then the primary agency's staff would need to be greater in number and variety. For instance, in the field of biomaterials it would take a battery of synthetic polymer chemists to carry the entire program, not just one.

The pattern of business arrangement between NHLI and such a primary institution could not fruitfully be a contractual one because of the heavy enphasis upon basic scientific research and the lack of expertise within NHLI to guide or monitor same. Consideration has been given to the possibility that this might be a Research and Demonstration Center, but the implication here is that demonstration is to be directed toward those who are primary deliverers of patient care rather than to scientific investigators.. The program would appear to this author to be most satisfactorily fitted either to the pattern of a program project grant, or to that of a Specialized Center of Research, or to that of a consortium grant as proposed in the revision of "Guide to Grant and Award Programs of NIH (DHEW Publication (NIH) 73-33, discussed in Executive Staff Meeting, NHLI, Feb. 25, 1974). One of the latter two would appear to be more appropriate because one or the other would provide greater flexibility and because it could be reviewed on the basis of the overall objective rather than on the basis of a series of individual smaller programs each of which could be approved or delected upon review. In terms of the obstacles listed at the beginning of Section 7, such an arrangement would handle them in the the following fashion:

1. There would be a sufficient number of monitors insofar as they are necessary within the primary agency.

2. There would be an assured availability of the necessary expertise in depth.

3. There would be adequate salaries to attract the top intellects into the field.

4. There would be an abundant opportunity for these individuals to have a personal involvement in the work in progress.

5. The scientific staff could be spared the mechanical administrative chores which are the bane of the existence of so many scientists within the NIH staff.

6. The primary agency would be free to dismiss those who are ineffective or uncooperative and to seek truly appropriate individuals to replace them.

7. The work would be heavily concentrated in the laboratories of the primary agency, thus doing away with the disadvantages of having activities widely sprinkled around the country.

8. There would be no restrictions on travel to visit possible subcontractors or workers holding grants

9. The concentration of all of this work in one area would facilitate the setting up of a retrieval system for data and developments, and scientific intercourse among the components of the project would be facilitated.

10. The pattern of organization proposed would do much to facilitate adequate interdisciplinary collaboration

11. Organization and operation of the primary agency by scientists of the expertise outlined should provide excellent assurance of avoidance of extravagant, iterative, scientifically unproductive animal experimentation.

12. This arrangement removes the scientific monitor from the whirlwind of crises which so regularly besets the Federal bureaucrat and leaves him undisturbed and able to keep his eye in constant fashion on the scientific problems to be solved.

13. This arrangement would offer the hope of employment of the expertise of members of the SCOR or consortium grantee consistently in the capacities for which they can be most fruitful.

IX. Recommendations

As a result of this overview, the following steps are recommended:

1. Recognition that there is too much unaccomplished basic scientific investigation to render fruitful the use of systems engineering in contracts to the exclusion of grants.

2. Discontinuance of efforts to accomplish basic scientific investigation under contract

3. Establishment of at least one Specialized Center of Research (SCOR) or a consortium grant for the further prosecution of the program on the artificial heart. This SCOR should be staffed with the full breadth and depth of expertise needed for the whole program and should be empowered to consummate subcontracts with industrial concerns when this is judged fruitful by the scientific staff of the SCOR and to make subgrants in areas in which this appears to that staff to be necessary.

4. Transferral to this SCOR or consortium grantee of the basic scientific investigative work now being attempted under contract

5. Transferral of the letting of contracts to this SCOR or consortium grantee for the routine research and development in the program.*

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*There are precedents for this move although not in the area of basic scientific investigation. One is the giving to TRW of the full responsibility for technical direction in development of the Minuteman rocket. A further example is the giving to Aerospace Corporation the same kind of freedom in contracts with the Department of Defense. A third is the recently consummated contract between the National Cancer Institute and Battelle Laboratories of Columbus, Ohio, in relation to the determination of toxicity of anticancer drugs, announced 4/15/74.

X. Summary

1. Research and development under systems engineering have blossomed in those areas in which the basic technology has been well in hand. This in general has been true of the thermal and electrical engines and in the development of electronic circuitry for control insofar as the basic physiology has been understood. It has fallen short in areas in which the basic scientific knowledge had still to be gained, as in physiological responses, rheology, and materials of appropriate longevity and compatibility with tissues and components of blood.

2. The programs on the artificial heart and on mechanical circulatory support have been too often hindered by lack of adequate numbers of personnel and expertise within the National Heart and Lung Institute.

3. The contractual pattern with direction from monitors in the National Heart and Lung Institute who have too often lacked the experience and expertise for this function appears to have been an important factor in militating against the engagement of the strongest possible investigators and developers.

4. The programs have cost $80,309,365 since inception. It is doubtful whether the fruits of the program have justified that cost.

5. Basic scientific investigation in many areas must be accomplished before the stated aims can be achieved. The goal-oriented contractual pattern of management (systems engineering) is simply not suitable for the accomplishment of such basic scientific investigation.

6. The recommendation is made that a large SCOR or a consortium grant (or perhaps two, one for biomaterials and one for all in the program, but biomaterials) be established with a fully adequate staff in terms of numbers and areas of expertise, truly competitive salaries, and authorization and funding to consummate subcontracts and subgrants where it is judged by the scientific staff of the SCOR or consortium grant to do so.

N.B. This page was re-done May, 1975.

Note:

The present Evaluation was submitted to NHLI on Nov. 29, 1974. After some time for review, it was returned to the author by the Acting Director/NHLI with a request that further documentation of specific statements in Section VII A be provided so as to be more secure in considering any of the changes in procedure recommended herein. There has been difficulty in gathering some of the data, and the author is immensely indebted to Dr. Sylvain Pitzele for his assistance in this matter.

All mention of various costs of the Artificial Heart Program refer to the costs up to the time of original submission of this Evaluation only.

ATTACHMENTS

1. Pages 8 through 11 of Report on Cardiac Replacement, 1969.
2. Supplemental Agreement with Thermo-Electron Corp., Mar. 1, 1971.
3. Letter from Dr. Walter Bornhorst of TECO, April 25, 1975.
4. Page from Annual Report of Thermo-Electron, Aug., 1974 on Animal Survival.
5. Blue Sheet: Continued study of the effects of added intracorporeal heat, and Request for noncompetitive contract renewal.
6. Internal memoranda on percutaneous leads, Dec. 10, 1974, and Feb. 5, 1975.
7. Internal evaluation of Veno-Arterial Bypass System, Jan. 19, 1973.
8. CDB's Criteria for Clinical Investigative Use of Left Ventricular Assist Devices, August 8, 1974.
9. Dennis memo on Consideration of Clinical Evaluation of LVAD, Oct. 12, 1974.
10. Memo of Sept. 18, 1972, about access to clinical facilities.
11. Memo of May 21, 1974, about Management Development Program.
12. Memo on conference with Dr. Walsh.

TABLES

CONSULTANTS

1. Stuart Bondurant, M.D., Vice President for Medical Affairs, Albany Medical College of Union University
2. Michael E. DeBakey, M.D., President, Baylor University College of Medicine
3. Lt. Col. Richard Coffee, Program Monitor for the Air Force for Rand Corporation and Analytic Service Corp.
4. Col. Russell D. Hensley, Ph. D., (Aeronautical Engineering, Stanford), Special Assistant to the Administrator, Office of Petroleum Allocation, Dept. of the Interior
5. Frederick Heydrick, M.D., Division of Extramural Affairs, NHLI
6. Lyman Moore, Executive Officer, NHLI
7. Vice-Admiral Eli T. Reich, U.S.N.
8. John Waldhausen, M.D., Chairman, Department of Surgery, Hershey School of Medicine of Pennsylvania State University
10. John B. Walsh, Ph. D., Deputy Director of Defense Research and Engineering (Strategic and Space Systems)
11. Vallee Willman, M.D., Chairman, Department of Surgery, St. Louis University School of Medicine

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6. AEC/NHLI Program Review, April 23, 1973. Minutes available in OD/NHLI. The material is being prepared for publication by the AEC.

7. National Council on Radiation Protection and Measurements. Report No. 39, issued Jan. 15, 1971.

8. C.H.Edmonds, D.A.Hughes, J.J.Migliore, W.J.Robinson, J.M.Fuqua, F.N.Huffman, and J.C.Norman. Nuclear Fueled Circulatory Support Systems, XIII: Neoplasm in Radiation Source Bearing Dog after 6 Years. Proceedings of the Alliance for Engineering in Medicine and Biology, Vol. 16, P. 4, Oct.7, 1974.

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